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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,492	01/23/2004	Fredric R. Bloom	IVGN 347	4921

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

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06/04/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/762,492	BLOOM ET AL.	
	Examiner	Art Unit	
	JaNa Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-13,77-79,108-111 and 113-117* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-13,77-79,108-111 and 113-117* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment of March 3, 2010 has been entered. Claims 1,14-76, 80-107 and 112 are cancelled. Claims 2-3, 8, 77, 79 and 108 have been amended. Claims 2-13, 77-79, 108-111 and 113-117 are under consideration in this office action.

Withdrawal of Objections and Rejections

2. The following objections and rejections have been withdrawn in view of applicants' amendments:

a) The rejection of claims 2-14, 77-79 and 108-117 under 35 U.S.C. 102(b) as being anticipated by Short et al;

b) The rejection of claims 2-14, 77-79 and 108-117 under 35 U.S.C. 102(b) as being anticipated by Short et al;

c) The written description rejection of claims 2-14, 77-79 and 108-117 under 35 U.S.C. 112, first paragraph; and

d) The objection of claim 8.

Response to Arguments

3. Applicant's arguments with respect to claims 2-13, 77-79, 108-111 and 113-117 have been considered but are moot in view of the new ground(s) of rejection.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 2-13, 77-79, 108-111 and 113-117 are rejected under 35 U.S.C. 103(a) as being unpatentable over Short et al., (US Patent 5,510,099 published April 23, 1996) in view of Bloom et al., (WO 00/78925 dated December 28, 2000).

The claims are drawn to an isolated *Escherichia coli* strain W *(E. coli)* having a growth rate that is at least 5% greater than the growth rate of *E. coli* MM294, wherein said isolated *E. coli* does not contain genetic material of bacteriophage Wphi. The claims are also drawn to an isolated *E. coli* strain W having a growth rate that is at least 5% greater than the growth rate of *E. coli* MM294, wherein said isolated *E. coli* are does not contain genetic material of bacteriophage Mu.

Short et al., teach a prolysogenic microorganism contains an isolated bacteriophage cI gene operably linked to expression control elements (col. 15, lines 19-25). Preferably the microorganism is a strain of *E. coli* (col. 15, lines 26-28). The prolysogen is phage-free, i.e., is free of genetic material recoverable via a bacteriophage packaging extract (col. 15, lines 46-48). Preferably the strain of *E.coli* is deficient in one or more of the mcrA, mcrB, mrr, hsdR restriction systems and the like

(col. 15, lines 49-52). The commercially available *E.coli* strain has the following genotype: recA1, endA1, mcrA, Δ(mcrBC-hsdRMS-mrr), Δ(argF-lac)U169, phi80ΔlacZΔM15, Tn10(tet^r) (col. 28, lines 61-64). SCS-8 provides the lacZΔM15 gene which allows for alpha-complementation (col. 28, lines 64-66). The ΔM15 portion of lacZ gene provided by the host is provided either episomally via a low copy number plasmid or F-factor or stably integrated into the bacterial chromosome (col. 29, lines 50-53). By removing these restriction systems, rescue efficiencies have been increased up to at least 12,000 pfu/ug genomic DNA (col. 26, lines 25-27). Of course, one skilled in the art will recognize that "removal" of these restriction systems may be effected by deleting or inhibiting the activity of these restriction systems and the term "restriction system deficient" systems includes, but is not limited to, removal of the restriction systems; additionally naturally occurring strains of *E.coli* that are deficient in these systems may be isolated and used (col. 26, lines 24-34). Table 1 shows rescue efficient using *E.coli* strains with different restriction genotypes including *E.coli* C (col. 26-27, lines 57-14). Short et al., teach a phage-free, prolysogenic strain of *E. coli* (see claim 7). However Short et al., do not teach strain W.

Bloom et al., teach rapidly growing *E. coli* strain W that lacks endogenous plasmids, and teaches strains BRL3781, BRL3784 and *rec*A- derivatives (page 3, lines 23-28). Bloom et al., teach strains wherein the modification includes alterations of the *rec*A$^-$ genotype such as *rec*A1/*rec*A13 or *rec*A deletions, a *lacZ*$^-$ genotype that allows for alpha complementation such as *lac*X74 *lacZΔM15* or other *lac*Z deletions a protease deficient genotype such as *Δ*lon and/or ompT$^-$, an endonuclease minus genotype such

as endA1, a genotype suitable for M13 phage infection by including the F' episome, a restriction negative, modification positive genotype such as *hsd*R17(r_K^-, m_K^+), a restriction negative, modification negative genotype such as *hsd*S20(r_B^-, m_B^-), a methylase deficient genotype such as *mcr*A and/or *mcr*B and/or *mrr*, a genotype suitable for taking up large plasmids such as *deo*R, a genotype containing suppressor mutations such as *sup*E and/or *sup*F. Bloom et al., teach other suitable modifications are known to those skilled in the art and such modifications are considered to be within the scope of the present invention (pages 4-5, lines 22-6). Bloom et al., teach the rapid growing bacteria that have an increased growth rate that is greater than 5%, 10%, 25%, 50%, 75%, 100%, 150%, 200% than the growth rate of the reference microorganism which is *E.coli* MM294 (as known as ATCC 33625) (page 10, lines 14-19). Bloom et al., teach compositions comprising the rapidly growing microorganisms (page 17, lines 30-32). Example 3 teaches the construction of BRL3582 a *recA*$^-$ *E.coli* W contained in broth. Example 4 teaches *E.coli* W derivatives lacking native plasmids contained in medium.

Therefore, it would have been prima facie obvious at the time of applicants invention to modify the *isolated E.coli strain* having a growth rate that is at least 5% greater growth rate and does not contain genetic material of bacteriophage Wphi or Mu as taught by Short et al., wherein the modification incorporates using strain W as taught by Bloom et al., in order provide a bacterial strain having a rapid growing rate that is greater than 5%, 10%, 25%, 50%, 75%, 100%, 150%, 200% than the growth rate of the reference microorganism which is *E.coli* MM294. Furthermore, there is a reasonable

expectation of success in incorporating the techniques of Short et al., to achieve a bacterial strain without the bacteriophages, since Short et al., teach that any strain of *E.coli* is deficient in one or more of the mcrA, mcrB, mrr, hsdR restriction systems and Bloom et al., provides a strain that is a deficient in *mcr*A and/or *mcr*B and/or *mrr*, especially when no change in their respective functions, thus the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Furthermore, the claim would have been obvious because the mutation techniques were recognized as part of the ordinary capabilities of one skilled in the art.

5. Claims 2-13, 77-79, 108-111 and 113--117 are rejected under 35 U.S.C. 103(a) as being unpatentable over Short et al., (US Patent 5,955,056 published September 21, 1999) in view of Bloom et al., (WO 00/78925 dated December 28, 2000).

The claims are drawn to an isolated *Escherichia coli (E. coli)* having a growth rate that is at least 5% greater than the growth rate of *E. coli* MM294, wherein said isolated *E. coli* does not contain genetic material of bacteriophage Wphi. The claims are also drawn to an isolated *E. coli* having a growth rate that is at least 5% greater than the growth rate of *E. coli* MM294, wherein said isolated *E. coli* are does not contain genetic material of bacteriophage Mu.

Short et al., teach a prolysogenic microorganism contains an isolated bacteriophage cI gene operably linked to expression control elements (col. 15, lines 4-7). Preferably the microorganism is a strain of *E.coli* (col. 15, line 13). The prolysogen is

phage-free, i.e., is free of genetic material recoverable via a bacteriophage packaging extract (col. 15, lines 30-33). Preferably the strain of *E.coli* is deficient in one or more of the mcrA, mcrB, mrr, hsdR restriction systems and the like (col. 15, lines 33-39). Short et al., teach no restriction systems found in *E.coli* K12 (col. 15, line 38-39). The SCS-8 commercially available *E.coli* strain has the following genotype: recA1, endA1, mcrA, Δ(mcrBC-hsdRMS-mrr), Δ(argF-lac)U169, phi80ΔlacZΔM15, Tn10(tet^r) (col. 28, lines 44-49). SCS-8 provides the lacZΔM15 gene which allows for alpha-complementation (col. 28, lines 47-49). The ΔM15 portion of lacZ gene provided by the host is provided either episomally via a low copy number plasmid or F-factor or stably integrated into the bacterial chromosome (col. 29, lines 32-35). By removing these restriction systems, rescue efficiencies have been increased up to at least 12,000 pfu/ug genomic DNA (col. 26, lines 14-18). Of course, one skilled in the art will recognize that "removal" of these restriction systems may be effected by deleting or inhibiting the activity of these restriction systems and the term "restriction system deficient" systems includes, but is not limited to, removal of the restriction systems; additionally naturally occurring strains of *E.coli* that are deficient in these systems may be isolated and used (col. 26, lines 16-23). Table 1 shows rescue efficient using *E.coli* strains with different restriction genotypes including *E.coli* C (col. 26, lines 45-63). Short et al., teach a phage-free, prolysogenic strain of *E.coli* (see claim 12d). However Short et al., do not teach strain W.

Bloom et al., has been discussed above as teaching a rapidly growing *E. coli* strain W that lacks endogenous plasmids.

Therefore, it would have been prima facie obvious at the time of applicants invention to modify the *isolated E.coli strain* having a growth rate that is at least 5% greater growth rate and does not contain genetic material of bacteriophage Wphi or Mu as taught by Short et al., wherein the modification incorporates using strain W as taught by Bloom et al., in order provide a bacterial strain having a rapid growing rate that is greater than 5%, 10%, 25%, 50%, 75%, 100%, 150%, 200% than the growth rate of the reference microorganism which is *E.coli* MM294. Furthermore, there is a reasonable expectation of success in incorporating the techniques of Short et al., to achieve a bacterial strain without the bacteriophages, since Short et al., teach that any strain of *E.coli* is deficient in one or more of the mcrA, mcrB, mrr, hsdR restriction systems and Bloom et al., provides a strain that is a deficient in *mcr*A and/or *mcr*B and/or *mrr*, especially when no change in their respective functions, thus the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Furthermore, the claim would have been obvious because the mutation techniques were recognized as part of the ordinary capabilities of one skilled in the art.

Conclusion

6. No claims allowed.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Robert Mondesi, can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/
Examiner, Art Unit 1645

/Mark Navarro/

Primary Examiner, Art Unit 1645